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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,878	11/21/2005	Hiroshi Takahashi	0760-0346PUS1	9660

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EXAMINER	
GODDARD, LAURA B	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
05/14/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/533,878	TAKAHASHI ET AL.	
	Examiner	Art Unit	
	LAURA B. GODDARD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/4/08, 8/13/07, 4/16/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7 and 10-16* is/are pending in the application.

4a) Of the above claim(s) *11,12,15 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-7,10,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/16/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The supplemental elections filed February 4, 2008 and August 13, 2007, and Amendment filed April 16, 2007 in response to the Office Actions of November 2, 2007, July 13, 2007, and November 16, 2006, respectively, are acknowledged and have been entered. Applicants elected the species of "examining nucleic acids" and "HTLV-1 gene" with traverse. Applicants additionally elected the species of "leukemia cells" with traverse.

2. Applicants' traversal in the remarks mailed August 13, 2007, in response to the restriction mailed July 13, 2007 was addressed by Examiner in the Office Action mailed November 2, 2007.

3. Applicants argue in the remarks mailed February 4, 2008, p. 2, that the various cells as recited in claim 1 do not require a separate classification, do not have a separate status in the art, nor require a different field of search. Applicants argue that by searching on species, the Examiner is necessarily searching the other species since the species are so closely related in subject matter (e.g., the species are all cancer cells). Applicants argue it would not be undue search burden to search the entire scope of all the pending claims.

The arguments have been considered but are not found persuasive because as stated in the Office Action mailed November 2, 2007, p. 3: "The species are independent or distinct because each cell type has a different etiolology, different

structure, and different function, and expresses different proteins, all of which distinguish them as physiologically distinct tissues". Further, the species are independent or distinct because claims to the different species recite the mutually exclusive characteristics of such species. In addition, these species are not obvious variants of each other based on the current record. It would be undue search burden to examine all of the cell types as claimed. For these reasons, the restriction requirement is deemed to be proper and is therefore made FINAL.

4. Claims 1-3, 5-7, 10-16 are pending. Previously pending claims 1 and 5 have been amended. New claims 11-16 were added. Claims 11, 12, 15, and 16 are withdrawn as being drawn to a non-elected species. Claims 1-3, 5-7, 10, 13, and 14 are currently being examined.

NEW REJECTION

(based on new considerations)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3, 5-7, 10, 13, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (J Cancer Res Clin Oncol, 2001, 127:489-494) in view of WO 93/06117 (Wands et al, published April 1993, IDS), Suzuki et al (Blood, 1999, vol.

94, p. 98a, supplement1, part 1; abstract #430, IDS), and Takemoto et al (Blood, 1994, 84:3080-3085).

The claims are drawn to a method for examining a sample containing cancer cells comprising contacting a sample comprising at least one type of cells selected from leukemia cells separated from a body, with magnetic beads utilizing antigen-antibody reaction between said cancer cells and an anti-SF-25 antibody or antigen-binding fragment thereof, then collecting said magnetic beads by magnetic force to collect cells bound to said magnetic beads, and examining said collected cancer cells which are bound to said magnetic beads, wherein cell binding to the magnetic beads is indicative of a cancer that expresses SF-25 antigen (claims 1 and 2), wherein said cancer cells are those contained in blood (claims 3 and 10), wherein said cancer cells are leukemia cells or leukemic mononuclear cells (claims 5 and 6), wherein the examination is of nucleic acids (claim 7), wherein said examination of nucleic acid include examination of HTLV-1 (claim 13), wherein said examination includes PCR (claim 14).

Park et al teach immunomagnetic beads coated with an antibody specific for a cancer antigen expressed by cancer cells and using said immunomagnetic beads for the separation and isolation of said cancer cells that express the antigen and examining the isolated cancer cells using RT-PCR (abstract, p. 490, col. 1 and 2). The cancer cells were separated from a human body and contained in blood (abstract; p. 490, col. 2). Park et al teach that immunomagnetic bead selection successfully isolates and concentrates cancer cells expressing the antigen recognized by the antibody comprised by the bead, provides a more sensitive method for RT-PCR analysis than regular RT-

PCR, and decreases chances of false positives in RT-PCR analysis (p. 493, col. 1). The immunobead RT-PCR assay relies on a preliminary isolation of tumor cells from body fluids, which is then followed by amplification of one or more mRNA markers by RT-PCR (p. 493, col. 1). Park et al teach that the feasibility and the prognostic value of immunobead RT-PCR assay, which combines the enrichment of cancer cells by immunomagnetic bead selection and the RT-PCR amplification of tumor-specific mRNAs, has been demonstrated in several studies of breast, prostate, and gastrointestinal cancers (p. 492, col. 2).

Park et al does not teach that the immunomagnetic beads utilize SF-25 antibody, examining leukemia cells, or examining the HTLV-1 gene.

Wands et al teach that the SF-25 antigen has been shown by immunohistochemical staining to be expressed by several human tumor types including leukemia (p. 6, line 29 through p. 7, line 8; p. 15, lines 1-12). Wands et al teach preparation of the SF-25 monoclonal antibody (p. 11, lines 23 through p. 12, line 13; p. 19-23) and using the SF-25 antibody to bind and detect tissue or SF-25 antigen in a sample including blood samples (p. 12, lines 14-22; p. 40-41). Wands et al teach that for immunodiagnostic assays, SF-25 antibody can be attached to various labels and to solid supports including magnetite, and the support material can be in the form of beads (p. 41, lines 6 to p. 42, line 2).

Suzuki et al teach that adult T-cell leukemia (ATL) cells highly express SF-25 antigen (abstract).

Takemoto et al teach examining peripheral blood mononuclear cell and lymph node cell samples of leukemic patients by using PCR to detect HTLV-1, which would be examining leukemic mononuclear cells (abstract; p. 3080, col. 1 through p. 3081, col. 1). Takemoto et al teach that detection of HTLV-1 can be used in the diagnosis of adult T-cell leukemia (ATL) (abstract; p. 3083, both columns; p. 3084, col. 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use immunomagnetic beads with SF-25 antibodies to isolate and examine leukemic cells using the immunomagnetic bead enrichment and nucleic acid examination method taught by Park et al because Wands et al and Suzuki et al teach that leukemia cells or ATL cells express SF-25 antigen and Wands et al teach that the SF-25 antibodies can be used in conjunction with magnetite and beads for immunodiagnostic assays. One would have been motivated to use immunomagentic SF-25 antibody isolation for examining leukemia mononuclear cells, or ATL cells, in order to enrich the sample cell population with leukemia cells for diagnostic examination and because Wands suggests the SF-25 can be attached to magnetite and beads for diagnostic examination of cancer cells expressing SF-25 antigen. One of ordinary skill in the art would have a reasonable expectation of success using the immunomagnetic beads with SF-25 antibodies to isolate and enrich a sample population of leukemia cells because Park et al demonstrate that immunomagnetic bead selection and enrichment is a known and successful method for isolating cancer cells expressing a specific antigen and Wands et al teach that cancer cells including leukemia cells expressing SF-25

antigen can be specifically bound by SF-25 antibody conjugated to magnetite and solid bead support for diagnostic assays.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to examine the HTLV-1 gene by PCR in the leukemia cell sample isolated by immunomagnetic beads in order to diagnose adult T-cell leukemia (ATL), as taught by Takemoto et al, and because Park et al teach that immunomagnetic bead-enriched cancer cells and be examined by PCR. One would have been motivated to examine the leukemia cell sample that is enriched in order to efficiently diagnose ATL so the patient can receive proper treatment, and because enriched cell populations yield higher sensitivity and specificity for nucleic acid examination. One would have a reasonable expectation of success in examining an enriched leukemia cell sample for HTVL-1 by PCR because Park et al demonstrate increased sensitivity and specificity for nucleic acid detection from cancer cells enriched by immunomagnetic bead selection and Takemoto demonstrate successful PCR examination of HTLV-1 nucleic acid in leukemic cells for diagnosis of leukemia.

Finally, the Supreme Court has determined, in *KSR International Co. v. Teleflex, Inc.*, 550 U.S._, 82, USPQ2d 1385 (2007), that ".....[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results" (KSR, 550 U.S. at_, 82 USPQ2d at 1395). The court further found that "..... the conclusion that when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious" (KSR,

550 U.S. at_, 82 USPQ2d at 1395-1396). Thus, when considering obviousness of a combination of known elements, the operative question is "whether the improvement is more than the predictable use of prior art elements according to their established functions" ((KSR, 550 U.S. at_, 82 USPQ2d at 1396).

Given the above, applying the same logic to the instant process claims, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the SF-25 antibody diagnostic magnetite beads of Wands et al for the immunobeads of Park et al, to isolate, enrich and examine leukemic cells because the prior art method of Park et al differs from the claimed method only by the substitution of the known technique of using SF-25 antibody on immunomagnetic beads for isolation of cancer cells expressing SF-25 antigen. Given that immunomagentic bead selection of cancer cells was conventional and well known in the art at the time the invention was made, wherein their functions were well known in the art, substitution of SF-25 antibodies into the method of Park et al to isolate leukemic cells expressing SF-25 antigen would have yielded predictable results to one of ordinary skill in the art at the time of the invention. The claims are obvious over the cited references because the results yielded would be no more than one would expect from such a substitution.

Further, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the HTVL-1 PCR examination of Takemoto et al for the RT-PCR examination of Park et al, to examine leukemic cells because the prior art method of Park et al differs from the claimed method only by the substitution of the known technique of examining leukemia cells for HTLV-1 by PCR for

the RT-PCR examination of cancer cells. Given that examining leukemia cells for HTLV-1 by PCR was conventional and well known in the art at the time the invention was made, wherein the function was well known in the art, substitution of examining leukemia cells for HTLV-1 by PCR into the method of Park et al to examine leukemia cells and diagnose leukemia would have yielded predictable results to one of ordinary skill in the art at the time of the invention. The claims are obvious over the cited references because the results yielded would be no more than one would expect from such a substitution.

6. All other rejections and objections recited in the Office Action mailed November 16, 2006 are hereby withdrawn. Applicants arguments in the remarks mailed April 16, 2007 are drawn to withdrawn rejections and are therefore moot.

7. **Conclusion:** No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA B. GODDARD whose telephone number is (571)272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Laura B Goddard, Ph.D./
Examiner, Art Unit 1642